

results obtained for the various carbon acid systems are consistent and we believe that the $\Delta\Delta pK$'s are significant.

Note first that the $\Delta\Delta pK$'s for MeO and PhO groups are negative in every instance, i.e., the observed ΔpK 's are smaller than those expected on the basis of the polar effect. This is a pattern that has been observed previously for the effect of α -MeO substituents on the base-catalyzed exchange rates for deprotonation of acetates, GCH_2CO_2Me , and their cyclic analogs.⁵ It has been suggested that, when $G = MeO$, the incipient carbanion produced in the transition state for these deprotonations is destabilized by an electronegativity effect and by lone pair-lone pair interactions.⁵ Such destabilizing effects by MeO or PhO in the carbanions, $MeOCH_2EWG^-$ and $PhOCH_2EWG^-$ would account for the negative $\Delta\Delta pK$ values in Table I.

In sharp contrast to the negative $\Delta\Delta pK$'s observed for PhO, the $\Delta\Delta pK$'s for PhS are all positive and large, ranging from 3.7 to 7.3 pK units. This suggests stabilization of the anions over and above that expected from a polar effect of the order of 6 to 10 kcal/mol. These effects are similar to those observed with strong π -acceptor groups,⁴ although they are somewhat smaller in magnitude.

The strikingly large acidifying effect of the PhS group can be brought out further by some direct comparisons of the pK data. Despite the much smaller polar effect of PhS ($\sigma_I = 0.30$) than Me_3N^+ ($\sigma_I = 0.82$), $PhSCH_2SO_2Ph$ is only 0.9 pK unit less acidic than $Me_3N^+CH_2SO_2Ph$, $PhSCH_2CN$ is only 0.2 pK unit less acidic than $Me_3N^+CH_2CN$, and 9-PhS-fluorene (pK = 15.4) is 2.4 pK units more acidic than 9- Me_3N^+ -fluorene (pK = 17.8).

It is difficult to decide whether these large effects are caused solely by the high degree of polarizability of sulfur, as the ab initio calculations suggest,³ or whether a conjugative effect is also operative. Several results from our pK data lead us to believe that more than polarizability is involved. Note, for example, that $\Delta\Delta pK$ is greater for $PhSCH_2COPh$ (3.7) than for $PhSeCH_2COPh$ (2.9), despite the greater polarizability of selenium. In addition, Hammett correlations for equilibrium acidities in Me_2SO in both the meta- and para-substituted phenylacetone nitrile system⁶ and the 3-substituted fluorene system,⁷ require σ_p^- for PhS, rather than σ_p , despite the fact that resonance effects are greatly attenuated when operating across a benzene ring.⁴ Finally, there is strong evidence that the F_3CSO_2 and $PhSO_2$ groups enter into conjugation based on their strong acidifying effect on methane and the diminution of this effect when the substituent is placed on a cyclopropane ring.⁸ Since tetravalent sulfur can exert strong conjugative effects, it seems likely that divalent sulfur can also enter into electron acceptor conjugation with α carbanions.

Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, and to the National Science Foundation (Grant MPS 74-12665) for support of this work. We wish to thank J. E. Bares, W. S. Matthews, and G. J. McCollum for some of the data in Table I.

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Received March 19, 1976

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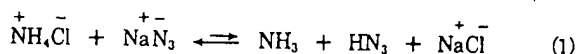
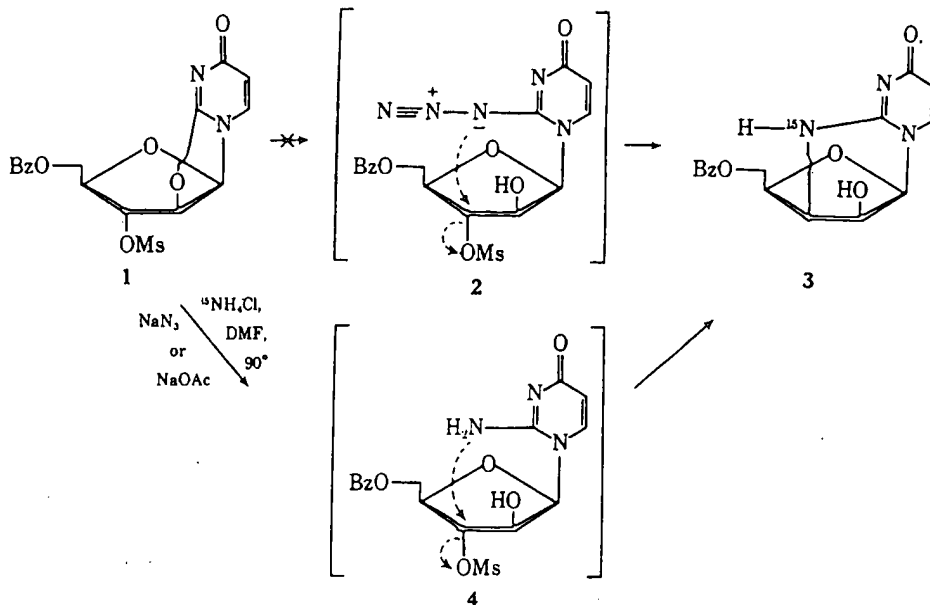
Nucleic Acid Related Compounds. 19. Concerning the Mechanism of Formation of "2,3'-Imino-1-(β -D-lyxofuranosyl)uracil" [2-Amino-1-(3-deoxy- β -D-lyxofuranosyl)- 4-pyrimidinone- $N^2 \rightarrow 3'$ -anhydronucleoside] from $O^2 \rightarrow 2'$ Cyclonucleosides and "Ammonium Azide"

Summary: Postulated attack of azide anion (from "ammonium azide") at C^2 of the pyrimidine ring of $O^2 \rightarrow 2'$ cyclonucleoside 1 followed by intramolecular cyclization with accompanying loss of nitrogen gas to give $N^2 \rightarrow 3'$ cyclonucleoside 3 does not occur, as was demonstrated by incorporation of ^{15}N from labeled ammonium chloride and verified by analogous formation of 3 using "ammonium acetate".

Sir: In a very recent issue of this journal, the conversion of $O^2 \rightarrow 2'$ -anhydro-1-(5-*O*-benzoyl-3-*O*-methanesulfonyl- β -D-arabinofuranosyl)uracil (1) and related $O^2 \rightarrow 2'$ cyclonucleosides to the corresponding $N^2 \rightarrow 3'$ -anhydro-2-amino-1-(5-*O*-benzoyl-3-deoxy- β -D-lyxofuranosyl)-4-pyrimidinone (3) and related derivatives using "ammonium azide" in hot *N,N*-dimethylformamide (DMF) was described.² This transformation was postulated to proceed via azide attack at C^2 of the pyrimidine ring followed by an unusual intramolecular attack by the geminal electrons of N^1 of the azide moiety (intermediate 2) to give 3 by an unexplained (necessarily reductive) process. Treatment of 5'-*O*-trityl- $O^2 \rightarrow 2'$ -anhydro-1-(β -D-arabinofuranosyl)uracil with "ammonium azide" in DMF at 110° was reported² to give 59% 1-(5-*O*-trityl-2-azido-2-deoxy- β -D-ribofuranosyl)uracil, plus 33% starting material, which is in agreement with previous studies of Moffatt and coworkers³ involving SN_2 -type displacement of O^2 from C^2 of an $O^2 \rightarrow 2'$ anhydronucleoside using lithium azide. An "unprecedented" "introduction of an azide group into pyrimidine bases through O^2 anhydronucleosides"² was proposed to explain the formation of 3. A "striking" "through bond" electronegative influence to C^2 was attributed² to the leaving group (mesylate) at C^3 to rationalize azide attack at C^2 in the 5'-*O*-trityl-3'-hydroxy compound (i.e., absence of the 3'-*O*-mesyl function).

Fox and coworkers⁴ have reported that treatment of 3'-*O*-mesyl- $O^2 \rightarrow 5'$ -anhydrothymidine with ammonia at room temperature in a sealed vessel gave the $N^2 \rightarrow 3'$ -anhydro-2',3'-dideoxy compound (corresponding to 3). Attack of ammonia at C^2 of the pyrimidine ring with displacement of alkoxide (OH_2C^5 or OCH_3 , from reaction with $MeOH/Et_3N$) was postulated with subsequent intramolecular displacement of mesylate by the exocyclic amino function of the isocytosine system to give the $N^2 \rightarrow 3'$ cyclonucleoside.⁴

In the present reaction, ammonium azide was assumed to be generated in situ from a sixfold molar excess of ammonium chloride and sodium azide.² This more soluble azide salt was the presumed nucleophile. However, the following acid-base equilibrium (eq 1) would be expected to provide a finite $[pK_a$



(NH_4Cl) = 9.25, pK_a (HN_3) = 4.72]⁵ steady-state concentration of ammonia, and Fox's results⁴ would suggest that reaction of ammonia with cyclonucleoside 1 might be very rapid in DMF at 90 °C.

Treatment of 1⁶ with 99 atom % ¹⁵N-ammonium chloride⁷ and ¹⁴N-sodium azide in DMF at 90 °C for 12 h and processing as described² gave 71% (65% recrystallized) 3: mp 258–260 °C (after the first crystallization), mp 285–286 °C (after recrystallization); uv (0.1 N HCl) max 232 nm (ϵ 17 000), sh 264 (6700), min 216 (12 000); uv (MeOH) max 217 nm (ϵ 32 600), sh 227, 262 (29 700, 4400) [lit.² mp 250–252 °C; uv (MeOH) max 217 nm (ϵ 33 300), sh 261 (4000); yield 70%]. The mass spectrum of this product had m/e 330.0974, calcd for M^+ ($\text{C}_{16}\text{H}_{15}^{14}\text{N}_2^{15}\text{NO}_5$) 330.0982. Comparison of mass spectra (AEI MS-50 with computer averaging of nine scans under identical conditions) of this product and a sample prepared using ¹⁴NH₄Cl indicated complete incorporation of ¹⁵N. Therefore, displacement of O² at the pyrimidine terminus of 1 by ammonia to give intermediate 4 followed by intramolecular cyclization to 3 is compatible with the labeling experiment. If this interpretation is correct, reaction of 1 with ammonium chloride and the salt of an acid of comparable strength with that of hydrazoic acid would be expected to proceed analogously. Acetic acid (pK_a = 4.76)⁵ and hydrazoic acid (pK_a ~ 4.72)⁵ are almost identical in acid strength. Treatment of 1 with an eightfold molar excess of ammonium chloride and sodium acetate in DMF at 90 °C under identical conditions with those above resulted in formation of 3 in 82% (72% recrystallized) yield. Thus, there is no evidence for formation of 2 or the implausible mechanism noted.²

Doerr and Fox⁸ have observed that 2-amino-1-(β -D-arabinofuranosyl)-4-pyrimidinone (1- β -D-arabinofuranosylisocytosine) is very easily (even during warming for recrystallization) converted to the O²→2'-anhydro uracil product by attack of the "up" O² at C² with evolution of ammonia. Therefore, ammonia displacement of oxygen at the pyrimidine terminus of the 3'-hydroxy-O²→2'-anhydro compound² (analogous to intermediate 4) would be unproductive since reversal to the O²→2' cyclonucleoside would be expected to proceed readily in DMF at 110 °C.⁸ In contrast, attack by azide at C² would lead to the observed² 2'-azido-2'-deoxy uracil nucleoside, presumably irreversibly. Thus, azide attack at C² of cyclonucleosides is the normal course³ and does not result from absence of a "through bond" electronegative ef-

fect² in the case of the 3'-hydroxy compound. All chemistry involved in these reactions is in harmony with precedents^{3,4,8} in the literature.

Acknowledgment. Generous support from the National Research Council of Canada (A 5890) and The University of Alberta is gratefully acknowledged.

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Received February 17, 1976

Synthesis of 3-Dialkylaminocyclopentadienones¹

Summary: The title compounds are prepared by condensation of 3,4-diazacyclopentadienone 3-oxides with ynamines. The regioselectivity of the reaction was proven by hydrolysis of the amines to cyclopentene-3,5-diones.

Sir: The cycloaddition chemistry of 3,4-diazacyclopentadienone oxides² and related compounds^{3,4} with acetylenes has previously been reported and involved deep-seated rearrangements which could be rationalized from a first-formed 1,3-dipolar cycloadduct. In contrast with these results we have now found that ynamines (2) condense with 3,4-diazacyclopentadienone 3-oxides (1) in a Diels–Alder sense to produce 3-dialkylaminocyclopentadienones (3) in good yields (60–70%). These are the first representatives of this group of compounds to be reported.

In a typical preparation addition of 1.1 equiv of ynamine 2 to a stirred solution of 1 (1 equiv) in CH₂Cl₂ led to an exo-